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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/933,559	08/20/2001	Veerappa S. Subramanian	4961-5	6556

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EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/933,559	SUBRAMANIAN ET AL.	
	Examiner	Art Unit	
	Micah-Paul Young	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment of Papers Received: Response/Amendment filed 03/11/04.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Lowey (USPN 4,680,323 hereafter referred to as '323), Baker et al (USPN 4,687,660 hereafter to as '660) and Seth (USPN 6,033,686 hereafter to as '686). The claims are again drawn to a solid dosage form of bupropion HCl. The dosage form is a sustained release tablet and the composition comprises carboxyvinyl polymer and microcrystalline cellulose or lactose. In addition the stabilization profile discussed above, after 2 weeks of storage at 55 degrees Celsius, there is at least 90% w/w of the bupropion remaining in the composition. The carboxyvinyl polymer provides a release profile where the drug is released from a period of 8 to

24 hours. Applicant recites a specific profile where the drug is release in a particular percentage at a particular time (i.e. 30 – 45% within 1 hour, 60 – 80% in 4 hours, etc.). Claim 9 recites a method of stabilizing the drug comprising combining the constituents, and granulating with purified water.

The '323 patent discloses a pharmaceutical tablet comprising pharmaceutically active agents, carboxyvinyl polymer and other cellulose derivates as excipients. Various classes of pharmaceutical agents are useful in the formulation including analgesics and bronchodilators (Abstract). The carboxyvinyl polymer allows for the active agents to be released over a 24-hour period (col. 3, lin. 55-60). The carboxyvinyl polymer is present in a concentration of from 1-90% (claims). What is lacking in the reference is a disclosure of the particular active agent, bupropion hydrochloride, and the other excipients recited by the claims, microcrystalline cellulose and/lactose.

'660 et al discloses a bupropion hydrochloride composition comprising water-soluble and insoluble polymers such as cellulose derivatives. The composition further comprises lactose (examples).

The '686 patent however discloses a sustained release tablet comprising bupropion HCl, a water insoluble, water-permeable film-forming polymer and water-soluble polymer. The tablet releases 30 – 60% of the bupropion HCl after 1 hour, 55 – 80% after 2 hours, 75 – 95% after 3 hours, and 80 – 100% after 4 hours (col. 3, lin. 40 – 56). '686 also discloses a method of preparing the composition comprising mixing the constituents and granulating with purified water (examples). Though the reference does not explicitly claim this process as stabilizing, Seth's final product is a stable tablet.

With regard to applicant's limitation that the carboxyvinyl polymer is the sole stabilizing and control releasing material, it is the position of the examiner that this limitation cannot be given patentably weight without a showing of criticality. The combination proposed discloses a formulation comprising a carboxyvinyl polymer. Burden is shifted to applicant to provide the criticality to the carboxyvinyl polymer acting as the sole polymer. The Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. *See Ex parte Phillips*, 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int. 1993), *Ex parte Gray*, 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

With these aspects in mind it would have been obvious to one of ordinary skill in the art to combine the teachings and suggestion of the art. A skilled artisan would have been motivated to combine the bupropion HCL of '660 into the formulation of '323 in order to impart stability and proper release of the agent. A skilled artisan would have been able to make the substitution since both references share excipients, active agents, and operate within the same field of endeavor. A skilled artisan would have been able to substitute the bupropion HCL of '660 into the formulation of '323, along with the lactose of the formulation in order the effect the release of the drug. Release profiles can be manipulated through concentrations of the non-active excipients, and is within the level of skill in the art. A skilled artisan would have further been motivated to combine the purified water and further excipients of '680 in order to better refine

the processing and release profile of the active agent. '680 releases bupropion HCL with ethyl cellulose as a possible excipient, similar to '660. A skilled artisan would have been motivated to make these combinations and substitutions in order to optimize the release of a bupropion HCL tablet. An expected result of such a combination would have been a tablet with a release profile and consistency useful as an anti-depressant.

Response to Arguments

1. Applicant's arguments filed 3/11/04 have been fully considered but they are not persuasive. Applicant argues that:

a. Applicant argues that since carboxyvinyl polymer is the sole stabilizer and rate-releasing agent in the formulation, while the combination of the prior art discloses a combination of stabilizers/rate controllers, the combination does not obviate the instant claims.

2. Regarding this argument, it is the position of the examiner that applicant has yet to provide evidence that supports such a limitation. Applicant has directed the examiners attention to the specification where carboxyvinyl polymer is described as the stabilizer and rate-controlling polymer (page 4, lin 1-6). The examiner now directs applicant to the following paragraph where lactose and microcrystalline cellulose are disclosed as being used for their rate controlling properties (page 4, lin. 7-11). Claims 12, and 13 include lactose and microcrystalline cellulose, yet limits their function since carboxyvinyl polymer acts as the sole stabilizer/rate controller. Applicant provides no examples where the carboxyvinyl polymer is the sole rate controller or stabilizer since each and every example includes lactose and/or microcrystalline cellulose. Further applicant argues that the release rates achieved by the instant invention are

achieved without the need for HPMC, and therefor must be at least patentable over at least the '323 patent. It is the position of the examiner that applicant has merely replaced one water-soluble polymer (HPMC) with another (microcrystalline cellulose) to achieve the release rate. It is well known that HPMC and microcrystalline cellulose have similar rate controlling properties and can be used interchangeably. Though the product is removed in the instant claims, the function remains and is well known to those of ordinary skill. Further applicant has not disclosed any adverse effects for the inclusion of HPMC into the formulation. Applicant must provide evidence that HPMC would negatively effect the release of the formulation in order to rule it out of the formulation. The prior art combination provides a bupropion HCl formulation comprising carboxyvinyl polymer, microcrystalline cellulose and lactose with a release profile useful in treating various disorders. For these reasons at least the claims remain obviated by the prior art.

Conclusion

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 571-272-0608. The examiner can normally be reached on M-F 7:00-4:30 every other Monday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Micah-Paul Young
Examiner
Art Unit 1615

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